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Research Paper

# Cardiothoracic Transplant Recipient *Mycoplasma hominis*: An Uncommon Infection with Probable Donor Transmission

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ABSTRACT

The role of infection with *Mycoplasma hominis* following cardiothoracic organ transplantation and its source of transmission have not been well-defined. Here, we identify and describe infection with *M. hominis* in patients following cardiothoracic organ transplantation after reviewing all cardiothoracic transplantations performed at our center between 1998 and July 2015. We found seven previously unreported cases of *M. hominis* culture positive infection all of whom presented with pleuritis, surgical site infection, and/or mediastinitis. PCR was used to establish the diagnosis in four cases. In two instances, paired single lung transplant recipients manifested infection, and in one of these pairs, isolates were indistinguishable by multilocus sequence typing (MLST). To investigate the prevalence of *M. hominis* in the lower respiratory tract, we tested 178 bronchoalveolar lavage (BAL) fluids collected from immunocompromised subjects for *M. hominis* by PCR; all were negative. Review of the literature revealed an additional 15 cases of *M. hominis* in lung transplant recipients, most with similar clinical presentations to our cases. We recommend that *M. hominis* should be considered in post-cardiothoracic transplant infections presenting with pleuritis, surgical site infection, or mediastinitis. *M. hominis* PCR may facilitate early diagnosis and prompt therapy. Evaluation for possible donor transmission should be considered.



## 1. Introduction

*Mycoplasma hominis* (*M. hominis*) is a mollicute that colonizes the urogenital tract and occasionally causes invasive disease. Extra-genital infections with this organism occur primarily in immunosuppressed persons. *M. hominis* has been linked to pregnancy-related complications and causes meningitis and pneumonia in neonates (Cassell et al., 1991; Samra et al., 2002; Waites et al., 1988). *M. hominis* is not visualizable by gram stain due to its lack of a cell wall, and although it may grow on standard aerobic or anaerobic bacterial culture plates, this method is insensitive and requires highly experienced laboratory personnel to recognize colonies of *M. hominis*. *M. hominis*-specific culture may be performed, but are not widely available, and even if they are available, is not rapid. The route of acquisition of *M. hominis* in patients who undergo cardiothoracic transplantation has not been defined. In two prior reports in *Chest* the authors speculated 1) the organism entered the bloodstream (though blood cultures were negative) of a lung transplant recipient who developed pleural and pulmonary infection with *M. hominis*. These authors speculated manipulation of the urinary tract with a Foley catheter elicited invasion of lung tissue damaged by transplantation (Lyon et al., 1997) and 2) an 18 year old women developed diffuse alveolar hemorrhage following bone marrow transplant due to unproven airway or urinary tract colonization (Kane et al., 1994). Herein, we describe seven new cases of *M. hominis* infection in cardiothoracic transplant recipients and review the literature on the topic. We highlight the unique clinical presentation of *M. hominis* in this patient population and present evidence suggesting that this infection may be donor-transmitted. *M. hominis* should be considered in the etiological diagnosis of surgical site infections, mediastinitis and pleuritis after lung or heart-lung transplantation; use of *M. hominis*-specific PCR may expedite diagnosis.

## 2. Methods

The study was reviewed and approved by the Mayo Clinic Institutional Review Board (14-007214). Individual patient consent was not needed.

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### 2.1. Case Detection

Using our heart and lung transplant database and chart review (between 1998 and July 2015) we found seven (among 182 lung transplants and heart-lung performed and 453 heart transplants) previously unreported cases of culture positive *M. hominis* infection in cardiothoracic transplant recipients (Table 1). In each case routine cultures grew *M. hominis* and no other bacterial pathogens were identified. PCR for *M. hominis* (beginning January 2014), *Ureaplasma urealyticum*, and *Ureaplasma parvum* (beginning January 2015) were requested when suspected infection sites were gram stain negative, and early bacterial cultures were negative with the presence of white blood cells. *M. hominis*, *Ureaplasma urealyticum*, and *Ureaplasma parvum* PCR were specifically performed prospectively on all donor airway specimens beginning in 2015. Importantly, in each case reported herein *M. hominis* was the only infectious agent identified. None of these *M. hominis* cases developed hyperammonemia and none of these cases tested positive for *Ureaplasma* sp. However, we have recently identified a single case of donor bronchus which tested as *M. hominis* PCR negative and *Ureaplasma urealyticum* PCR positive as well as a single case of donor bronchus which tested as *M. hominis* PCR positive and *Ureaplasma urealyticum* PCR negative. Both cases were treated prophylactically without evidence of disease. All *M. hominis* cases and donor surveillance cases were reported to the host organ procurement organization as required by the Organ Procurement Transplant Network. Prior to 2009 all patient received cytolytic induction, after 2009 only heart recipients received cytolytic induction. All patients received intraoperative methylprednisolone. Post-transplant immunosuppression is listed in Table 1.

### 2.2. Literature Review

PubMed was queried beginning in 1950 for *M. hominis* infection and cardiothoracic transplantation.

### 2.3. Surveillance Detection of *M. hominis* DNA in BAL Fluid from Non-cardiothoracic Transplant Immunocompromised Patients

BAL samples submitted for detecting organisms commonly found in immunocompromised hosts undergoing clinically indicated bronchoscopy were tested for *M. hominis* DNA. We used a previously-described real-time PCR assay targeting *M. hominis tuf* (Cunningham et al., 2013). DNA was extracted on the MagNA Pure LC instrument using the MagNA Pure total nucleic acid isolation kit (Roche Applied Science, Indianapolis, IN).

## 3. Results

### 3.1. Patient Evaluation and Donor Characteristics

All patients received standard immunosuppression. All patients had pre-transplant sputum cultures which were negative for *M. hominis*. Routine perioperative bacterial prophylaxis included Vancomycin for 48 h and Cefepime for 48–72 h. Trimethoprim/sulfamethoxasole was typically begun on post-operative day 2 or 3. Any additional bacterial prophylaxis was based upon donor and recipient airway cultures. In all cases clinical signs, including prolonged pleural effusion, prompted routine bacterial and fungal cultures of suspected sites of infection.

**Table 1**
Summary of 7 Mayo Clinic cases of *Mycoplasma hominis* infection in thoracic transplant recipients.

| Case tran-plant (year) | Age (years) Sex | Transplant indication | Transplant type Immune suppression | Signs or symptoms (days after transplant) | Clinical presentation | Method used to diagnose *M. hominis* infection | Surgical management | Antimicrobial therapy | Outcome |
|---|---|---|---|---|---|---|---|---|---|
| A (2000) | 44M | Secondary pulmonary hypertension | HL ATG/CSA/AZA/Pred | Sternal site infection with sternal dehiscence (15) | Sternal wound infection | Culture-positive surgical debridement specimens | Debridement and sternectomy | Doxycycline and ciprofloxacin × 10 years | Recovered |
| B (2009) | 69M | Idiopathic pulmonary fibrosis | SL ATG/Tacro/AZA/Pred | Dyspnea, unilateral pleural effusion (14) | Pleuritis | Culture positive pleural fluid | Catheter drainage of pleural fluid | Levofloxacin for 3 weeks | Recovered |
| C (2011) | 41F | Pulmonary hypertension | HL ATG/Tacro/Mycop/Pred | Dyspnea, cough with progression to circulatory shock in 48 h (19) | Mediastinitis with aortic anastomotic leak | Culture positive pericardial fluid, periaortic tissue and BAL fluid | Mediastinal debridement (3) | Clindamycin for 4 weeks then doxycycline (lifelong) | *Recovered* |
| D (2014) | 64M | Idiopathic pulmonary fibrosis | SL Tacro/AZA/Pred | Dyspnea, loculated pleural effusion (16) | Pleuritis | PCR- and culture-positive pleural fluid | Thoracotomy and debridement | Levofloxacin and doxycycline for 6 weeks, followed by doxycycline for 6 months | Slow recovery with multiple subsequent infectious complications |
| E (2015) | 64M | Chronic obstructive lung disease | SL Tacro/AZA/Pred | Fever, leukocytosis and a loculated hydropneumothorax (7) | Pleuritis | PCR- and culture-positive pleural fluid; culture positive debridement specimens (multiple) | Thoracotomy and debridement, wound VAC | Doxycycline (lifelong) | Recovered |
| F (2015) | 70M | Idiopathic pulmonary fibrosis | SL (same donor as D) Tacro/AZA/Pred | Dyspnea, and loculated pleural effusion (21) | Pleuritis | PCR- and culture-positive pleural fluid; culture-positive central venous catheter tip | Pleural fluid aspiration | Doxycycline (lifelong) | Recovered |
| G (2015) | 63M | Idiopathic pulmonary fibrosis | BL Tacro/Myco/Pred | Subcutaneous emphysema (63) | Right bronchial anastomotic leak | PCR positive from both pretransplant donor bronchi and recipient pleural fluid; culture positive from both pretransplant donor brochi and later bronchial anastomotic eschar | Delayed bronchial anastomotic healing | Levofloxacin and doxycycline (lifelong) | Recovered |

M, male; F, female; HL, heart-lung transplant; BL, bilateral lung transplant; SL, single lung transplant; BAL, bronchoalveolar lavage; ATG, antithymocyte globulin; Tacro, tracrolimus; AZA, azathioprine; Pred, prednisone; Myco, mycophenolate mofetil.